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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,072	07/02/2001	Stephen W. Scherer	086671/0113	2291

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EXAMINER
EINSMANN, JULIET CAROLINE

ART UNIT	PAPER NUMBER
1634	12

DATE MAILED: 12/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,072	SCHERER ET AL.	
	Examiner	Art Unit	
	Juliet C Einsmann	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *7-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6 and 20-22* is/are rejected.

7)☒ Claim(s) *2-6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in Paper No. 11 is acknowledged. The traversal is on the ground(s) that the examination of at least claims 1-6, 20-22, and 7-16 could be performed without serious search burden. This is not found persuasive because under the PCT rules, a showing of lack of unity is required for proper restriction of claims and such a showing has been made. Furthermore, however, it would indeed pose a serious burden on the examiner to examine claims 1-6, 20-22, and 7-16 all together.

MPEP 801 states,

> "This chapter is limited to a discussion of the subject of restriction and double patenting under Title 35 of the United States Code and Title 37 of the Code of Federal Regulations as it relates to national applications filed under 35 U.S.C. 111(a). **The discussion of unity of invention under the Patent Cooperation Treaty Articles and Rules as it is applied as an International Searching Authority, International Preliminary Examining Authority, and in applications entering the National Stage under 35 U.S.C. 371 as a Designated or Elected Office in the U.S. Patent and Trademark Office is covered in Chapter 1800** (emphasis added)."

Referring to Chapter 1800, MPEP 1893.03(d) states,

> "The principles of unity of invention are used to determine the types of claimed subject matter and the combinations of claims to different categories of invention that are permitted to be included in a single international or national stage patent application. The basic principle is that an application should relate to only one invention or, if there is more than one invention, that applicant would have a right to include in a single application only those inventions which are so linked as to form a single general inventive concept. A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes **over the prior art** (emphasis added)."

In the instant case, there is not unity of invention between the products of group I and claims 7-16 because the products of group I are anticipated by the prior art (see rejections under 102 set forth herein).

Furthermore, it is noted, however, that Applicant's assertions regarding the burden of the search and examination of claims 1-6, 20-22, and 7-16 are not persuasive. As a first point, applicant sets forth no reasoning or arguments to support the assertion. Second, the two groups of claims would be separately classified in the US classification system (in 536/23.1 and 435/6, for example), and the separate classification of groups I and II is *prima facie* evidence that the examination of these inventions would place an undue burden on the examiner. Furthermore, the searches required to examine the instantly claimed methods and the instantly claimed nucleic acids would be different, requiring a search of different classes, different electronic databases and the use of different key words in such a search.

The requirement is still deemed proper and is therefore made FINAL.

2. Preliminary amendments filed 1/19/01 and 7/2/01 have been entered. Claims 1-6 and 2-22 are under examination herein.

Priority

3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

4. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-6 and 20-22 of this application. Applicant claims priority to two provisional applications, 60/092,495, filed 7/20/98 and 60/130,269, filed 4/21/99. Neither of these provisional applications provide adequate support for claims 1-6 and 20-22.

The '495 application does not provide descriptive support or enabling disclosure for nucleic acid molecules containing a sequence encoding a protein tyrosine phosphatase which is associated with Lafora's disease. While the '495 application contains verbatim support for such a claim (see at least claim 1 in the '495 provisional application), the '495 application does not fully describe or enable such a claim. This lack of support under 35 U.S.C. 112 is fully discussed in the rejections herein. Furthermore, it is noted that the '495 application does provide written description of instant SEQ ID NO: 3 and SEQ ID NO: 5 (figures 7 and 9, respectively), but these do not provide adequate support for a claim to nucleic acid molecules containing a sequence encoding a protein tyrosine phosphatase which is associated with Lafora's disease.

The '269 application disclosed only primers for diagnostic tests and fails to provide any further descriptive support nucleic acid molecules containing a sequence encoding a protein tyrosine phosphatase which is associated with Lafora's disease. Particularly, the '269 application does not disclose SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5.

Thus, the filing date of claims 1-6 and 20-22 for examination herein is considered to be the international filing date, 20 July 1999.

Claim Objections

5. Claims 2, 3, 4, 5, and 6 are objected to because of the following informalities:

These claims all refer to figures. MPEP 2173(s) states "Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." In the instant case the isolated nucleic acids can be referred to using SEQ ID numbers. Furthermore, claims 4-6 are not in compliance with the sequence rules because they refer to particular nucleic acid sequences but to not use proper sequence identifiers.

Appropriate correction is required.

6. Applicant is advised that should claim 4 be found allowable, claim 5 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof because the sequences shown in figure 4A and in figure 7 are the same sequence (i.e. SEQ ID NO: 3). When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 3 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 3, the phrase "preferably" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention.

Claim 3 is indefinite because part (d) refers to itself when it recites "which will hybridize to (a) and (d) under," and this is confusing. Furthermore, claim 3 is confusing in part (d) when it recites "under stringent hybridization conditions" because it is not clear how this recitation is intended to limit the claim, since all hybridization conditions are stringent to some degree.

Claim 22 is indefinite over the recitation of "capable of hybridizing" because capability is a latent characteristic and the claims do not set forth the criteria by which to determine capability. That is, it is not clear whether the recited nucleic acids have the potential to hybridize or do in fact hybridize the recited sequences. Amendment of the claim to read, for example, "which hybridizes" would obviate this rejection.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 3-6, and 20-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, and 3-6 are directed to isolated nucleic acid molecules containing a sequence encoding a protein tyrosine phosphatase which is associated with Lafora's disease. Claim 1 is generic in nature, reciting functional language with no recitation of a structure for the claimed nucleic acids. Claims 3-6 include language claiming sequences that are "homologous" to a given structure, that are fragments of SEQ ID NO: 1 and hybridize to SEQ ID NO: 1 or a homologue of SEQ ID NO: 1 under stringent hybridization conditions, that comprise SEQ ID NO: 3 (sequence in Fig. 4A and 7), or that comprise SEQ ID NO: 5 (sequence in Fig. 9). Claims 20-22 recite isolated nucleic acid molecules that have recited percent identities to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 or that hybridize to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 under recited hybridization and wash conditions. However, the instant specification only describes a single full length sequence encoding a protein tyrosine phosphatase which is associated with Lafora's disease, that is SEQ ID NO: 1. The specification describes two additional nucleic acids that are associated with Lafora's disease, SEQ ID NO: 3 and SEQ ID NO: 5.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of instant SEQ ID NO: 1 which is a full length cDNA encoding a protein that has the signature protein tyrosine phosphatase domain (see Denu et al. Cell, Vol. 87, pages 361-364 and instant Figure 4C). Applicant is also in possession of two alternate

transcripts that comprise portions of SEQ ID NO: 1, namely SEQ ID NO: 3 and SEQ ID NO: 5. The specification teaches that these two transcripts are incomplete coding sequences, noted particularly because they do not have ATG start sites (see p. 25). Thus, it is not clear if these sequences actually encode active protein tyrosine phosphatases, even though they contain the "signature domain," it is not known from the teachings of the specification if the missing portions of encoded protein are essential for proper folding of the protein and thus tyrosine phosphatase activity. The specification teaches that there are mutations associated with Lafora's disease in each of SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5 (see Figure 3, for example, where SEQ ID NO: 1 is the consensus sequence, SEQ ID NO: 3 is transcript A and SEQ ID NO: 5 is transcript B). The subject matter which is claimed is described above.

The specification does not provide any written description as to how instant SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 can be modified and still retain their association with Lafora's disease or their ability to encode a tyrosine phosphatase. The specification and prior art provide a "signature domain" for proteins that are tyrosine phosphatases, but neither provide any guidance as to how instant SEQ ID NO: 1 can be modified but still retain its ability to encode a protein tyrosine phosphatase, furthermore, the claims do not even require that this signature domain remain in tact or be included in any of the claimed nucleic acids.

Instant claim 1, in particular, has a complete absence of any structural description of the claimed nucleic acid. Thus, it encompasses any nucleic acids encoding protein tyrosine phosphatases that may be associated with Lafora's disease, including additional homologues and variants of the instantly disclosed protein tyrosine phosphatase undescribed herein, as well as other proteins yet undiscovered that have the same function and are related to the disease.

Furthermore, claim 2 encompasses fragments that share as little as 15 base pairs with instant SEQ ID NO: 1, provided they encode a protein tyrosine phosphatases that is be associated with Lafora's disease. The specification does not provide any guidance as to how to obtain additional sequences that fall within this genus. Claims 20-22, while providing for a structural definition of the claimed nucleic acids do not provide a proper structure to function relationship to defined the claimed genus. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention.

With regard to the written description, all of these claims encompass nucleic acid sequences different from those disclosed in the specific SEQ ID No:s which, for claims 6 and 20-22 include modifications by permitted by the % identity language, homologue language, and hybridization language for which no written description is provided in the specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the nucleic acid sequence of the disclosed SEQ ID Nos are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception or written description of nucleic acid encoding a protein tyrosine phosphatases that is associated with Lafora's disease which has nucleic acids modified by addition, insertion, deletion, substitution or inversion with respect to SEQ ID NO: 1 but retaining correlative function in the claimed product. Nor has the specification provided any no record or description which would demonstrate conception or written description of nucleic acids that are associated with Lafora's disease which has nucleic acids modified by addition, insertion, deletion, substitution or inversion with respect to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 but retaining correlative function in the claimed product.

11. Claims 1, 3-6, and 20-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a protein tyrosine phosphatase which is associated with Lafora's disease wherein the nucleic acid sequence comprises instant SEQ ID NO: 1, OR for nucleic acids associated with Lafora's disease wherein the nucleic acids consist of instant SEQ ID NO: 3 or instant SEQ ID NO: 5, does not reasonably provide enablement for additional nucleic acids that are associated with Lafora's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1 and 3-6 are directed to isolated nucleic acid molecules containing a sequence encoding a protein tyrosine phosphatase which is associated with Lafora's disease. Claim 1 is

generic in nature, reciting functional language with no recitation of a structure for the claimed nucleic acids. Claims 3-6 include language claiming sequences that are "homologous" to a given structure, that are fragments of SEQ ID NO: 1 and hybridize to SEQ ID NO: 1 or a homologue of SEQ ID NO: 1 under stringent hybridization conditions, that comprise SEQ ID NO: 3 (sequence in Fig. 4A and 7), or that comprise SEQ ID NO: 5 (sequence in Fig. 9). Claims 20-22 recite isolated nucleic acid molecules that have recited percent identities to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 or that hybridize to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 under recited hybridization and wash conditions.

The specification teaches a single full length sequence encoding a protein tyrosine phosphatase which is associated with Lafora's disease, that is SEQ ID NO: 1. The specification describes two additional nucleic acids that are associated with Lafora's disease, SEQ ID NO: 3 and SEQ ID NO: 5. The specification teaches that instant SEQ ID NO: 1 is a full length cDNA encoding a protein that has the signature protein tyrosine phosphatase domain (page 25 and Figure 4C). Applicant is also in possession of two alternate transcripts that comprise portions of SEQ ID NO: 1, namely SEQ ID NO: 3 and SEQ ID NO: 5. The specification teaches that these two transcripts are incomplete coding sequences, noted particularly because they do not have ATG start sites (see p. 25). Thus, it is not clear if these sequences actually encode active protein tyrosine phosphatases, even though they contain the "signature domain." It is not known from the teachings of the specification if the missing portions of encoded protein are necessary for proper folding of the protein and thus tyrosine phosphatase activity. The specification teaches that there are mutations associated with Lafora's disease in each of SEQ ID NO: 1, SEQ ID NO:

3, and SEQ ID NO: 5 (see Figure 3, for example, where SEQ ID NO: 1 is the consensus sequence, SEQ ID NO: 3 is transcript A and SEQ ID NO: 5 is transcript B).

The specification does not provide any guidance as to how instant SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 can be modified and still retain their association with Lafora's disease and/or their ability to encode a tyrosine phosphatase. The specification and prior art provide a "signature domain" for proteins that are tyrosine phosphatases (see Denu et al. Cell, Vol. 87, pages 361-364), but neither provide any guidance as to how instant SEQ ID NO: 1 can be modified but still retain its ability to encode a protein tyrosine phosphatase, furthermore, the claims do not even require that this signature domain remain in tact or be included in any of the claimed nucleic acids.

The identification of additional nucleic acids of fragments of the instantly disclosed nucleic acids which retain association with Lafora's disease and/or encode polypeptides that retain tyrosine phosphatase activity is highly unpredictable. The activity of a protein is dependent on the folding of the polypeptide chain, and the location of the active site relative to the rest of the protein (see for example, Denu et al. who describe the structure of protein tyrosine phosphatases). Small changes in the amino acid sequence of a polypeptide can disrupt this folding and thus the ability of a polypeptide to function. Additionally, it is highly unpredictable what sequences of nucleic acid will be associated with a particular disease. In order to identify additional sequences, the ordinary pracitioner would be required to undertake analysis of many many patients to screen for additional sequences whose presence is an indicator of disease.

In light of the lack of guidance in the specification and prior art, the lack of additional working examples, the high level of unpredictability in the field of the invention and the high

quantity of experimentation necessary to practice the claimed invention, it is concluded that undue experimentation would be required to practice the claimed invention commensurate in scope with the instant claims.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 22 is rejected under 35 U.S.C. 102(b) as being anticipated by Bartnik et al. (EP 0705842).

Bartnik et al. teach an isolated nucleic acid that would hybridize to a nucleic acid sequence set forth in SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5 under the stringency conditions recited in the claims. The nucleic acid TAU10(1) taught by Bartnik et al. has 98.9% similarity with instant SEQ ID NO: 1 over nucleotides 2669-2849 of instant SEQ ID NO: 1.

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Qy    2669 GGAGATGACATTTGCTTTGGGCAGAGGCAGCTAGCCAGGACACATTTCCACTATAATTTT 2728
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 GGAGATGACATTTGCTTTGGGCAGAGGCAGCTAGCCAGGACACATTTCCACTATAATTTT 60

Qy    2729 ACAAAGTTAAATTTATAAGCTAGCATTAAGTAAAGTGAAG-TCCAGCTCCCTTGCTAAAA 2787
           |||||||||||||||||||||||||||||||||||||||| ||||||||||||||||||
Db      61 ACAAAGTTAAATTTATAAGCTAGCATTAAGTAAAGTGAAGTTCCAGCTCCCTTGCTAAAA 120

Qy    2788 ATAACTAGAGGTAATAATTGGTATTCAGGTAACTCATTTACAGTCATAATGTGTTGTGAA 2847
           |||||||||||||||||||||||||||||||||||||||| ||||||||||||||||||
Db     121 ATAACTAGAGGTAATAATTGGTATTCAGGTAACTCATTTACA-TCATAATGTGTTGTGAA 179

Qy    2848 AA 2849
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Db 180 AA 181

In the alignment, the top sequence is a portion of instant SEQ ID NO: 1, and the bottom sequence is TAU10(1). The TAU10(1) sequence has 98.9% local similarity over nucleotides 2481-2661 of instant SEQ ID NO: 3, and 96.4% local similarity over nucleotides 466-631 of instant SEQ ID NO: 5. Such a nucleic acid would hybridize to any one of SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5 under the recited conditions.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

14. Claims 1, 3, 20, 21, and 22 are rejected under 35 U.S.C. 102(a) as being anticipated by Serratosa et al. (Human Molecular Genetics, Feb. 1999, Vol. 8, No. 2).

This reference is a 102(a) reference against these claims because the claims were not granted priority back to the provisional applications. Thus, the filing date of these claims is the instant filing date, 20 July 1999.

Serratosa et al. provide an isolated nucleic acid that is associated with Lafora's disease and encodes a putative protein tyrosine phosphatase (p. 346 and Fig. 4). Serratosa et al. teach an isolated nucleic acid that has 88.5% identity with instant SEQ ID NO: 1. The nucleic acid taught by Serratosa et al. is described as a "composite sequence" of a number of cDNA transcripts, and was deposited in GenBank under accession AJ130763 (Fig. 2). For Applicant's convenience, the GenBank record is provided. Nucleotides 1-2805 of nucleic acid taught by Serratosa et al. share 99.8% identity with SEQ ID NO: 1 over nucleotides 242-2805 of instant SEQ ID NO: 1.

```
  Query Match             88.5%;  Score 2767.2;  DB 9;  Length 2805;
  Best Local Similarity   99.8%;  Pred. No. 0;
  Matches 2802;  Conservative    0;  Mismatches    3;  Indels    3;  Gaps    3;

Qy     242 TGGACACGTTCTGGTACAAGTTCCTGAAGCGGGAGCCGGGAGGAGAGCTCTCCTGGGAAG 301
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 TGGACACGTTCTGGTACAAGTTCCTGAAGCGGGAGCCGGGAGGAGAGCTCTCCTGGGAAG 60

Qy     302 GCAATGGACCTCATCATGACCGTTGCTGTACTTACAATGAAAACAACTTGGTGGATGGTG 361
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db      61 GCAATGGACCTCATCATGACCGTTGCTGTACTTACAATGAAAACAACTTGGTGGATGGTG 120

Qy     362 TGTATTGTCTCCCAATAGGACACTGGATTGAGGCCACTGGGCACACCAATGAAATGAAGC 421
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 TGTATTGTCTCCCAATAGGACACTGGATTGAGGCCACTGGGCACACCAATGAAATGAAGC 180

Qy     422 ACACAACAGACTTCTATTTTAATATTGCAGGCCACCAAGCCATGCATTATTCAAGAATTC 481
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 ACACAACAGACTTCTATTTTAATATTGCAGGCCACCAAGCCATGCATTATTCAAGAATTC 240

Qy     482 TACCAAATATCTGGCTGGGTAGCTGCCCTCGTCAGGTGGAACATGTTACCATCAAACTGA 541
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 TACCAAATATCTGGCTGGGTAGCTGCCCTCGTCAGGTGGAACATGTTACCATCAAACTGA 300

Qy     542 AGCATGAATTGGGGATTACAGCTGTAATGAATTTCCAGACTGAATGGGATATTGTACAGA 601
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     301 AGCATGAATTGGGGATTACAGCTGTAATGAATTTCCAGACTGAATGGGATATTGTACAGA 360

Qy     602 ATTCCTCAGGCTGTAACCGCTACCCAGAGCCCATGACTCCAGACACTATGATTAAACTAT 661
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     361 ATTCCTCAGGCTGTAACCGCTACCCAGAGCCCATGACTCCAGACACTATGATTAAACTAT 420

Qy     662 ATAGGGAAGAAGGCTTGGCCTACATCTGGATGCCAACACCAGATATGAGCACCGAAGGCC 721
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     421 ATAGGGAAGAAGGCTTGGCCTACATCTGGATGCCAACACCAGATATGAGCACCGAAGGCC 480

Qy     722 GAGTACAGATGCTGCCCCAGGCGGTGTGCCTGCTGCATGCGCTGCTGGAGAAGGGACACA 781
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     481 GAGTACAGATGCTGCCCCAGGCGGTGTGCCTGCTGCATGCGCTGCTGGAGAAGGGACACA 540

Qy     782 TCGTGTACGTGCACTGCAACGCTGGGGTGGGCCGCTCCACCGCGGCTGTCTGCGGCTGGC 841
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     541 TCGTGTACGTGCACTGCAACGCTGGGGTGGGCCGCTCCACCGCGGCTGTCTGCGGCTGGC 600

Qy     842 TCCAGTATGTGATGGGCTGGAATCTGAGGAAGGTGCAGTATTTCCTCATGGCCAAGAGGC 901
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     601 TCCAGTATGTGATGGGCTGGAATCTGAGGAAGGTGCAGTATTTCCTCATGGCCAAGAGGC 660

Qy     902 CGGCTGTCTACATTGACGAAGAGGCCTTGGCCCGGGCACAAGAAGATTTTTTCCAGAAAT 961
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     661 CGGCTGTCTACATTGACGAAGAGGCCTTGGCCCGGGCACAAGAAGATTTTTTCCAGAAAT 720

Qy     962 TTGGGAAGGTTCGTTCTTCTGTGTGTAGCCTGTAGCTGGTCAGCCTGCTTCTGCCCCCTC 1021
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     721 TTGGGAAGGTTCGTTCTTCTGTGTGTAGCCTGTAGCTGGTCAGCCTGCTTCTGCCCCCTC 780

Qy    1022 CTGATTTCCCTAAGGAGCCTGGGATGATGTTGGTCAAATGACCTAGAAACAAGGATTCTA 1081
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     781 CTGATTTCCCTAAGGAGCCTGGGATGATGTTGGTCAAATGACCTAGAAACAAGGATTCTA 840

Qy    1082 CCTGAACTGAAAGGACTGTGTGACCTCCCCAAGCCAACCACTTTCACCTGGGATGACTTT 1141
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     841 CCTGAACTGAAAGGACTGTGTGACCTCCCCAAGCCAACCACTTTCACCTGGGATGACTTT 900

Qy    1142 CGATTATGCTTTGGTTTGGGGCTGTATTTTTGAAATACTCTACAAGAAAGCTGTGGCTCA 1201
           |||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||
Db     901 CGATTATGCTTTGTTTTGGGGCTGTATTTTTGAAATACTCTACAAGAAAGCTGTGGCTCA 960

Qy    1202 ACACATGAGAAGAAGCACGAAGCAGTTAGGCTGTACATCAGACAGAAGGGTAATGCGTGC 1261
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     961 ACACATGAGAAGAAGCACGAAGCAGTTAGGCTGTACATCAGACAGAAGGGTAATGCGTGC 1020

Qy    1262 AGTTCCTGCTGCCTGCAGGCAGACGAGGCCTTTGCTTTACAGCACTGTATGTGTTGCACG 1321
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    1021 AGTTCCTGCTGCCTGCAGGCAGACGAGGCCTTTGCTTTACAGCACTGTATGTGTTGCACG 1080

Qy    1322 ATGGATCCGTGACAGCACTTTCCTGTTGCACTGAAACTCTTGGCCATGTAGAGGAAAAGA 1381
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Db    1081 ATGGATCCGTGACAGCACTTTCCTGTTGCACTGAAACTCTTGGCCATGTAGAGGAAAAGA 1140

Qy    1382 TATGGAGTTATGTGGATTTCATCACTAGTATGTGTGCCGTGAGCTGGTCAGTTGCCAAAG 1441
Db    1141 TATGGAGTTATGTGGATTTCATCACTAGTATGTGTG-CGTGAGCTGGTCAGTTGCCAAAG 1199

Qy    1442 GAGGAAATAAGGTTAGAAGCCTGAACCGTTACAAAAGAAGAGCTCACTATGGTCAAAAAG 1501
Db    1200 GAGGAAATAAGGTTAGAAGCCTGAACCGTTACAAAAGAAGAGCTCACTATGGTCAAAAAG 1259

Qy    1502 TGATGGCTTTCAGGACTTGTTTTTTATCCTGCCTCACAGTTGTTAAAGTCTGTTCCAAGG 1561
Db    1260 TGATGGCTTTCAGGACTTGTTTTTTATCCTGCCTCACAGTTGTTAAAGTCTGTTCCAAGG 1319

Qy    1562 CATCACCTTCCTTCTCTACCCAACAACCCTGTGTAACAACTAAAGTAGAATTATCTCTCA 1621
Db    1320 CATCACCTTCCTTCTCTACCCAACAACCCTGTGTAACAACTAAAGTAGAATTATCTCTCA 1379

Qy    1622 TTTGTTGGTGGTTTTTCCTCAAAATTACCAAACAAAGCAAAAAATACCCTTGTTTTTTAT 1681
Db    1380 TTTGTT-GTTGTTTTTCCTCAAAATTACCAAACAAAGCAAAAAATACCCTTGTTTTTTAT 1438

Qy    1682 AGTTGAGATGTCAAGGAAGTTAAATTGAGGCTTAATGAGCATAGGTAGCTTGTCCAAGGT 1741
Db    1439 AGTTGAGATGTCAA-GAAGTTAAATTGAGGCTTAATGAGCATAGGTAGCTTGTCCAAGGT 1497

Qy    1742 CTCATGACCAGTCAAGGGCAAGCTGGAGTTAATAATCTATATTTATTTGACTCAGCACTG 1801
Db    1498 CTCATGACCAGTCAAGGGCAAGCTGGAGTTAATAATCTATATTTATTTGACTCAGCACTG 1557

Qy    1802 TTTTCATCACAACTTGTTTTCCCAGCATCATGTAGTGCATTTAGTTTTGTCTTTCTCAGG 1861
Db    1558 TTTTCATCACAACTTGTTTTCCCAGCATCATGTAGTGCATTTAGTTTTGTCTTTCTCAGG 1617

Qy    1862 GTATAGTCAATATGCCTGCAGGAGTTTCTATAGCGAGACATAGAATAGTATTCTGATCAG 1921
Db    1618 GTATAGTCAATATGCCTGCAGGAGTTTCTATAGCGAGACATAGAATAGTATTCTGATCAG 1677

Qy    1922 TTGCCAAAGAATCTAGGAAATTAGTTGTATTTTGTGCAAGCTAATTTAAAAACATGATGG 1981
Db    1678 TTGCCAAAGAATCTAGGAAATTAGTTGTATTTTGTGCAAGCTAATTTAAAAACATGATGG 1737

Qy    1982 GCTGTTTTAAGACCAGAGTGGAAATTCATGAGAGGAACTATACTACCAAAAGAGCCCAAA 2041
Db    1738 GCTGTTTTAAGACCAGAGTGGAAATTCATGAGAGGAACTATACTACCAAAAGAGCCCAAA 1797

Qy    2042 TGACCAAATCCATGGATAATTGCTTCACAGCCTTGGCCATCCTGGCTCAGCTCTCAATTT 2101
Db    1798 TGACCAAATCCATGGATAATTGCTTCACAGCCTTGGCCATCCTGGCTCAGCTCTCAATTT 1857

Qy    2102 AGTATAATATGCAGTTCCTGTGCCTCCAGACTATGCAGCTCATCACCCTAGGTTCTACAG 2161
Db    1858 AGTATAATATGCAGTTCCTGTGCCTCCAGACTATGCAGCTCATCACCCTAGGTTCTACAG 1917

Qy    2162 GAAATACAGAGATGAACAACTTTGCCTTCAAAAAATGTGCTGCCTAGAAAACAGACCTGC 2221
Db    1918 GAAATACAGAGATGAACAACTTTGCCTTCAAAAAATGTGCTGCCTAGAAAACAGACCTGC 1977

Qy    2222 ATTTCAACCCAACTGTAATGCAGGATTTGGACCATGAATGATATGCTAGAATAGAAGAAA 2281
Db    1978 ATTTCAACCCAACTGTAATGCAGGATTTGGACCATGAATGATATGCTAGAATAGAAGAAA 2037

Qy    2282 GAGAAGTGTTTTTTTAATTGAGAGCCTCTATGTGCAAGGTGATATATAATCATATCCAGT 2341
Db    2038 GAGAAGTGTTTTTTTAATTGAGAGCCTCTATGTGCAAGGTGATATATAATCATATCCAGT 2097
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Qy    2342 TTAATCTTCACAATATCCAATGAAGAAGGTCTCATTATCTCCATGATAAAGATGGGGAAA 2401
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2098 TTAATCTTCACAATATCCAATGAAGAAGGTCTCATTATCTCCATGATAAAGATGGGGAAA 2157

Qy    2402 CTAAGGTCAGAAGGGTTAACTCAACTGTCTATTGTCACATGATGAATAAATAGATGAAGT 2461
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2158 CTAAGGTCAGAAGGGTTAACTCAACTGTCTATTGTCACATGATGAATAAATAGATGAAGT 2217

Qy    2462 GAGATACAAAGCTGGGTTTGATTCAAAGCCCTTACTTTCCTAATTAAACTATGATGCGTA 2521
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2218 GAGATACAAAGCTGGGTTTGATTCAAAGCCCTTACTTTCCTAATTAAACTATGATGCGTA 2277

Qy    2522 TTTATTTTTCTGCACCTTCCTTTCTTCCACAAACACATATTGATAGATGCAAGAGACTCT 2581
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2278 TTTATTTTTCTGCACCTTCCTTTCTTCCACAAACACATATTGATAGATGCAAGAGACTCT 2337

Qy    2582 TATTTATAAGGCGTGGGGGACAAGAAGGATACAAGGTAAGTTTCAGTGGAGCTCAGAGGA 2641
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2338 TATTTAGAAGGCGTGGGGGACAAGAAGGATACAAGGTAAGTTTCAGTGGAGCTCAGAGGA 2397

Qy    2642 CGGGGAGATAGAACTGTGGCACTTAGGGGAGATGACATTTGCTTTGGGCAGAGGCAGCTA 2701
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2398 CGGGGAGATAGAACTGTGGCACTTAGGGGAGATGACATTTGCTTTGGGCAGAGGCAGCTA 2457

Qy    2702 GCCAGGACACATTTCCACTATAATTTTACAAAGTTAAATTTATAAGCTAGCATTAAGTAA 2761
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2458 GCCAGGACACATTTCCACTATAATTTTACAAAGTTAAATTTATAAGCTAGCATTAAGTAA 2517

Qy    2762 AGTGAAGTCCAGCTCCCTTGCTAAAAATAACTAGAGGTAATAATTGGTATTCAGGTAACT 2821
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2518 AGTGAAGTCCAGCTCCCTTGCTAAAAATAACTAGAGGTAATAATTGGTATTCAGGTAACT 2577

Qy    2822 CATTTACAGTCATAATGTGTTGTGAAAATTTAATCTTAAAAATTAAATTTTTAAACTATG 2881
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2578 CATTTACAGTCATAATGTGTTGTGAAAATTTAATCTTAAAAATTAAATTTTTAAACTATG 2637

Qy    2882 TGGGTCTGTGAATTTCTTTAATGTCTAAGAAATCCAGCTTCATAATTTCCATGATACAAA 2941
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2638 TGGGTCTGTGAATTTCTTTAATGTCTAAGAAATCCAGCTTCATAATTTCCATGATACAAA 2697

Qy    2942 GATCTTTTTTCAGGTGGATTTTTACCTTTGTTCCTTTTGCTCTGATAGACAAAATCAGTT 3001
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    2698 GATCTTTTTTCAGGTGGATTTTTACCTTTGTTCCTTTTGCTCTGATAGACAAAATCAGTT 2757

Qy    3002 TAGGACTATTAAAGAATGTTTTGGAATAAACTGTCTTTTTCCTCAATG 3049
           |||||||||||||||||||||||||||||||||||||||||||||||
Db    2758 TAGGACTATTAAAGAATGTTTTGGAATAAACTGTCTTTTTCCTCAATG 2805
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In the alignment, the nucleic acid marked "Qy" is instant SEQ ID NO: 1, and the nucleic acid marked "Db" is the nucleic acid provided by Serratosa et al. The same nucleic acid shares 93.7% identity with instant SEQ ID NO: 3, and 99.5% local similarity over nucleotides 54-2861 of instant SEQ ID NO: 3. With regard to SEQ ID NO: 5, the nucleic acid taught by Serratosa et al. has 98.5% local identity with SEQ ID NO: 5, when nucleotides 224-685 of the nucleic acid taught by Serratosa et al. are aligned with nucleotides 17-478 of instant SEQ ID NO: 5.

It is noted that Serratosa et al. postulate that this nucleic acid encodes a putative protein tyrosine phosphatase, but do not demonstrate the activity of such a protein. The examiner is unable to undertake such an analysis, as a laboratory is not available. The rejection is applied in the interest of compact prosecution since the teachings of the Serratosa et al. reference meet all of the structural limitations provided in the claims.

15. Claims 1, 3, 4, 5, 6, 20, 21, and 22 are rejected under 35 U.S.C. 102(a) as being anticipated by Minassian et al. (Nature Genetics, Volume 20, pages 171-174, October 1998).

It is noted that the authorship of the Minassian et al. reference is distinct from the inventorship of the instant application and that this rejection may be overcome by the filing of a 132 Katz-type declaration.

This reference is a 102(a) reference against these claims because the claims were not granted priority back to the provisional applications. Thus, the filing date of these claims is the instant filing date, 20 July 1999.

Minassian et al. provide an isolated nucleic acid that is associated with Lafora's disease and encodes a putative protein tyrosine phosphatase (p. 172, Fig. 4c). Minassian et al. a nucleic acid sequence identical to the nucleotide sequence in instant figure 4A, see their Figure 4A. Additionally, teach an isolated nucleic acid comprising transcript B, which is identical to the isolated nucleic acid whose sequence is given in instant figure 9 (see their Figure 3 and Figure 4 and the figure legend of Fig. 4).

The nucleotide sequence provided by Minassian et al. would hybridize under conditions of high stringency with instant SEQ ID NO: 1, and comprise at least 15 bases of instant SEQ ID NO: 1. No alignment of instant SEQ ID NO: 1 to the sequence provided in Minassian et al. is

available, but at least nucleotides 189-597 of instant SEQ ID NO: 1 are identical to nucleotides 1-408 of the sequence taught in Figure 4A of the disclosure of Minassian.

It is noted that Minassian et al. postulate that this nucleic acid encodes a putative protein tyrosine phosphatase, but do not demonstrate the activity of such a protein. The examiner is unable to undertake such an analysis, as a laboratory is not available. The rejection is applied in the interest of compact prosecution since the teachings of the Minassian et al. reference meet all of the structural limitations provided in the claims.

Conclusion

16. Instant SEQ ID NO: 1 is free of the prior art. Claim 2 would therefore be allowable if all of the limitations of claim 1 were incorporated and if the objections to the claim set forth previously were overcome.

17. Claims drawn to isolated nucleic acids that are associated with Lafora's disease wherein the nucleic acids consist of instant SEQ ID NO: 3 or instant SEQ ID NO: 5 would meet the written description and enablement requirements, because these sequences have mutations in them that are associated with Lafora's disease, and thus one would know how to make and use them to detect Lafora's disease.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C. Einsmann
Examiner
Art Unit 1634

December 19, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600